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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,166	08/31/2001	David R. Elmaleh	MGA-003.01	1584
25181	7590	04/09/2007	EXAMINER	
FOLEY HOAG, LLP			VIVLEMORE, TRACY ANN	
PATENT GROUP, WORLD TRADE CENTER WEST			ART UNIT	PAPER NUMBER
155 SEAPORT BLVD				1635
BOSTON, MA 02110				
			MAIL DATE	DELIVERY MODE
			04/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

<b>Application No.</b>	<b>Applicant(s)</b>
09/945,166	ELMALEH ET AL.
<b>Examiner</b>	<b>Art Unit</b>
Tracy Vivlemore	1635

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 21 March 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
- a)  The period for reply expires 6 months from the mailing date of the final rejection.
  - b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2.  The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a)  They raise new issues that would require further consideration and/or search (see NOTE below);
  - (b)  They raise the issue of new matter (see NOTE below);
  - (c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-8, 10, 11 and 25-34.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

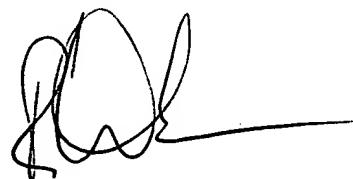
**REQUEST FOR RECONSIDERATION/OTHER**

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.
12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_
13.  Other: \_\_\_\_\_.

TV  
April 3, 2007

Continuation of 11. does NOT place the application in condition for allowance because: Applicants traverse the new matter rejection by arguing the specification provides support for a wide variety of constructs and that example 7 provides an assay for determining whether an antisense based construct crosses the blood brain barrier. Applicants further argue that example 6 teaches that intake and retention in tissues is related to the antisense rather than the sense properties of the construct and conclude that based on these examples a correlation of structure and function has been provided. This is not persuasive because example 6 compares retention of sense and antisense oligonucleotides in types of cells but does not address the relative abilities of these two types of oligonucleotides to cross the blood brain barrier and therefore this example provides no indication that the antisense portion dictates the construct's ability to cross the blood brain barrier. Further, as described in the original new matter rejection, the basis of the rejection is that the specification does not specifically contemplate that constructs comprising a targeting moiety as recited in the claims which do not cross the blood-brain barrier are part of the invention. The skilled artisan would not be led to envision which of the genus of compounds encompassed by the claims would not cross the blood-brain barrier based solely on the failure of the exemplified embodiment to do so.

Applicants traverse the art rejections of record by arguing there is no evidence that not crossing the blood brain barrier is an inherent feature of the claimed constructs. However, in applicants' traversal of the new matter rejection in the reply filed 6/26/06 they argue one example of an antisense conjugated to a radionuclide is sufficient to describe constructs that do not cross the blood brain barrier because inability to cross this barrier is a readily recognized property of such constructs, indicating that the lack of ability to cross the blood brain barrier in fact is an inherent property.



RICHARD SCHNIZER, PH.D.  
PRIMARY EXAMINER